

(FILE 'HOME' ENTERED AT 14:15:24 ON 04 DEC 2001)

FILE 'BIOSIS, EMBASE, CAPLUS, MEDLINE' ENTERED AT 14:15:50 ON 04 DEC 2001

L1 2092 S TRANSGENIC RAT?
L2 1527 S BRAIN CAPILLARY ENDOTHELIAL CELL?
L3 6 S L1 AND L2
L4 4 DUP REM L3 (2 DUPLICATES REMOVED)

d 14 1-4 ti abs ibib

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2001 ACS

TI Immortalized **brain capillary endothelial**
cell lines expressing PDGF receptor .beta. and angiopoietin-1

AB Immortalized **brain capillary endothelial**
cell lines TR-PCT1 expressing PDGF receptor .beta. and
angiopoietin-1 are disclosed. Use of the cell lines for drug screening
based on activity or expression of marker proteins such as PDGF receptor
.beta., Thy-1, ICAM-1, or angiopoietin-1 is claimed. Evaluation of cell
proliferation or calcium deposition on matrix can be use for screening as
well. The cell lines were derived from cerebrum of **transgenic**
rats harboring temp.-sensitive simian virus 40 large T-antigen
gene.

ACCESSION NUMBER: 2001:602486 CAPLUS

DOCUMENT NUMBER: 135:192516

TITLE: Immortalized **brain capillary**
endothelial cell lines expressing
PDGF receptor .beta. and angiopoietin-1

INVENTOR(S): Iisasa, Hisashi; Hattori, Kenshi; Nakajima, Emi;
Terasaki, Tetsuya; Obinata, Masuo

PATENT ASSIGNEE(S): Foundation for Scientific Technology Promotion, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001224367	A2	20010821	JP 2000-37827	20000216
WO 2001060984	A1	20010823	WO 2001-JP1016	20010214

W: CA, US

RW: CH, DE, FR, GB

PRIORITY APPLN. INFO.:

JP 2000-37827 A 20000216

L4 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS

TI Conditionally immortalized cell lines as a new in vitro model for the
study of barrier functions.

AB Conditionally immortalized brain and retinal capillary endothelial and
choroid plexus epithelial cell lines were established from a
transgenic rat (Tg rat) and mouse (Tg mouse) harboring
the temperature-sensitive simian virus 40 (ts SV 40) large T-antigen.
These cell lines exhibit temperature-sensitive cell growth due to the
expression of ts SV 40 large T-antigen. Mouse brain (TM-BBB) and rat brain
(TR-BBB) and rat retinal (TR-iBRB) capillary endothelial cell lines appear
to have a spindle-fiber shaped morphology and exhibit the typical
endothelial markers, such as von Willebrand factor and acetylated
low-density lipoprotein uptake. These cell lines express in vivo influx
and efflux transporters, such as P-glycoprotein (P-gp) and GLUT1, which is
capable of 3-O-methyl-D-glucose transport. TM-BBB cells are able to
undergo efflux transport of cyclosporin A, which is a substrate for P-gp
transport activity. They may also express oatp2 and exhibit
dehydroepiandrosterone sulfate and digoxin uptake activity. TR-BBB cells
express the mRNA of multidrug resistance associated protein 1 (MRP1) and a
large neutral amino acid transporter, which consists of LAT1 and 4F2hc.
TR-iBRB cells exhibit pH-dependent L-lactic acid transport activity and
express the mRNA of monocarboxylate transporter (MCT) 1 and 2. The choroid
plexus epithelial cell line (TR-CSFB) has polygonal cell morphology,
expresses the typical choroid plexus epithelial cell marker,
transthyretin, and has Na⁺, K⁺-ATPase located on the apical side. TR-CSFB

cells also exhibit amino acid transport activity which has been observed in vivo. These barrier cell lines established from the Tg rat and Tg mouse have in vivo transport functions and are good in vitro models for drug transport to the brain and retina and as a screen for drugs which might be capable of delivery to the brain and retina.

ACCESSION NUMBER: 2001:187383 BIOSIS
DOCUMENT NUMBER: PREV200100187383
TITLE: Conditionally immortalized cell lines as a new in vitro model for the study of barrier functions.
AUTHOR(S): Terasaki, Tetsuya (1); Hosoya, Ken-ichi
CORPORATE SOURCE: (1) Department of Molecular Biopharmacy and Genetics, Graduate School of Pharmaceutical Sciences, Aoba, Aramaki, Aoba-ku, Sendai, 980-8578: terasaki@mail.pharm.tohoku.ac.jp Japan
SOURCE: Biological & Pharmaceutical Bulletin, (February, 2001) Vol. 24, No. 2, pp. 111-118. print.
ISSN: 0918-6158.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English

11-14
102(a)

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2001 ACS
TI Preparation of established cell lines from transgenic animals carrying large T-Ag of a temperature-sensitive mutant of SV40
AB Described are the established cell lines prepd. from the retinal capillary endothelial cells, choroid plexus epithelial cells or **brain capillary endothelial cells** of a **transgenic rat** carrying a large T antigen gene of an SV40 temp. sensitive mutant tsA58. The cell line derived from the retinal capillary endothelial cells expresses the temp. sensitive SV40 large T antigen, the GLUT-1 carrier and the p-glycoprotein. The cell line derived from the choroid plexus epithelial cells expresses the temp. sensitive SV40 large T antigen gene and shows the localization of Na⁺-K⁺ ATPase and the GLUT-1 carrier in the cell membrane. When cultured in a monolayer, it shows the localization of Na⁺-K⁺ ATPase in the apical side. The cell line derived from the **brain capillary endothelial cells** expresses the temp. sensitive SV40 large T antigen, the GLUT-1 carrier, the p-glycoprotein, alk. phosphatase, and .gamma.-glutamyltransferase. A method for establishing immortalized cell lines by subculturing cells obtained from the retinal capillary endothelial cells, choroid plexus epithelial cells or **brain capillary endothelial cells** of the above described transgenic animal is claimed. These cells are useful in screening drugs regarding the safety or efficacy thereof and developing methods for the diagnosis or treatment of diseases relating to nutritional metab. in retinal tissues and brains at the cellular level.

ACCESSION NUMBER: 2000:241507 CAPLUS
DOCUMENT NUMBER: 132:276303
TITLE: Preparation of established cell lines from transgenic animals carrying large T-Ag of a temperature-sensitive mutant of SV40
INVENTOR(S): Hosoya, Kenichi; Terasaki, Tetsuya; Ueda, Masatsugu; Obinata, Masuo
PATENT ASSIGNEE(S): Ys New Technology Institute Inc., Japan
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

priority
claimed
to him

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000020599	A1	20000413	WO 1999-JP5423	19991001
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, FI, FR, GB, IT, NL, SE				
EP 1118664	A1	20010725	EP 1999-970124	19991001
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL, SE, FI				
PRIORITY APPLN. INFO.:			JP 1998-296138	A 19981002
			JP 1998-296139	A 19981002
			WO 1999-JP5423	W 19991001

REFERENCE COUNT: 7
REFERENCE(S):

- (1) Gillies, M; Investigative Ophthalmology & Visual Science 1997, V38(3), P635 MEDLINE
 - (2) Hakvoort, A; Journal of Neurochemistry 1998, V71(3), P1141 CAPLUS
 - (3) Hoheisel, D; Biochemical and Biophysical Research Communications 1998, V244(1), P312 CAPLUS
 - (5) Noble, M; Transgenic Research 1995, V4(4), P215 CAPLUS
 - (6) Ramanathan, V; Pharmaceutical Research 1996, V13(6), P952 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1
 TI mRNA expression and transport characterization of conditionally immortalized rat **brain capillary endothelial cell** lines; a new in vitro BBB model for drug targeting.
 AB **Brain capillary endothelial cell** lines (TR-BBB) were established from a recently developed **transgenic rat** harboring temperature-sensitive simian virus 40 (ts SV 40) large T-antigen gene (Tg rat) and used to characterize the endothelial marker, transport activity, and mRNA expression of transporters and tight-junction strand proteins at the blood-brain barrier (BBB). These cell lines expressed active large T-antigen and grew well at 33.degree.C with a doubling-time of about 22-31 hr, but did not grow at 39.degree.C. TR-BBBs expressed the typical endothelial marker, von Willebrand factor, and exhibited acetylated low-density lipoprotein uptake activity. Although the .gamma.-glutamyltranspeptidase activity in TR-BBBs was .apprx.3% of that of the brain capillary fraction of a normal rat, it was localized in the apical side, suggesting that it reflects the functional polarity of the in vivo BBB. The mRNA of tight-junction strand proteins such as claudine-5, occludin, and junctional adhesion molecule are expressed in TR-BBB13. Drug efflux transporter, P-glycoprotein, with a molecular weight of 170 kDa was expressed in all TR-BBBs and mdr 1a, mdr 1b, and mdr 2 mRNA were detected in TR-BBBs using RT-PCR. Moreover, mrp1 mRNA was expressed in all TR-BBBs. Influx transporter, GLUT-1, expressed at 55 kDa was revealed by Western blot analysis. It had 3-O-methyl-D-glucose (3-OMG) uptake activity which was concentration-dependent with a Michaelis-Menten constant of 9.86 .+- .1.20 mM. The mRNA of large neutral amino acid transporter, which consists of LAT-1 and 4F2hc was expressed in TR-BBBs. In conclusion, the conditionally immortalized rat **brain capillary endothelial cell** lines (TR-BBB) had endothelial makers, expressed mRNA for tight-junction strand proteins and the influx and efflux transporters and produced GLUT-1, which is capable of 3-OMG transport activity.

ACCESSION NUMBER: 2001153534 EMBASE
 TITLE: mRNA expression and transport characterization of conditionally immortalized rat **brain capillary endothelial cell** lines; a new in vitro BBB model for drug targeting.
 AUTHOR: Hosoya K.-I.; Takashima T.; Tetsuka K.; Nagura T.; Ohtsuki S.; Takanaga H.; Ueda M.; Yanai N.; Obinata M.; Terasaki T.
 CORPORATE SOURCE: Prof. T. Terasaki, Dept. of Mol. Biopharmacy/Genetics,

11-14
102(a)

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Journal of Drug Targeting, (2000) 8/6 (357-370).

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United Kingdom

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037 Drug Literature Index

039 Pharmacy

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English

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